

What is claimed is:

1. A method for inhibiting the growth of hormone-dependent tumor cells in a patient in need thereof, comprising administering to said patient a selective androgen receptor modulator in an amount effective therefor, wherein said selective androgen receptor modulator exhibits antagonist activity in said hormone-dependent tumor while exhibiting no activity or agonist activity against other, nontumor tissues containing the androgen receptor.
- 10 2. The method of claim 1, wherein said tumor cells are prostate tumor cells and wherein, in addition to exhibiting antagonist activity in said tumor cells and no activity or agonist activity against other, nontumor tissues containing the androgen receptor, said selective androgen receptor modulator further exhibits agonist, antagonist or no activity in normal prostate tissue.
- 15 3. The method of claim 1, wherein said selective androgen receptor modulator exhibits agonist activity against other, nontumor tissues containing the androgen receptor.
- 20 4. The method of claim 1, wherein said selective androgen receptor modulator exhibits no activity against other, nontumor tissues containing the androgen receptor.
5. The method of claim 1, wherein said hormone-dependent tumor is prostate cancer.
- 25 6. The method of claim 1, wherein said other, nontumor tissue containing the androgen receptor comprises one or more of the following tissues: seminal vesicles, male and female genitalia, skin, testis, ovary, cartilage, sebaceous glands, hair follicles, sweat glands, muscle, gastrointestinal vesicular cells, thyroid follicular cells, adrenal cortex, liver, pineal, bone, stromal cells, kidney tubules, urinary bladder and/or brain cortical and subcortical regions.
- 30 7. The method of claim 6, wherein said other, nontumor tissue containing the androgen receptor comprises one or more of the following tissues: cardiac muscle, skeletal muscle and/or smooth muscle.
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8. A selective androgen receptor modulator, which modulator exhibits antagonist activity in a hormone-dependent tumor while exhibiting no activity or agonist activity against other, nontumor tissues containing the androgen receptor.
- 5 9. A method for the treatment of a condition remediable by administration of the selective androgen receptor modulator of claim 8, comprising administering to a patient said selective androgen receptor modulator in an amount effective therefor, wherein said condition is selected from the following: hirsutism, acne, seborrhea, Alzheimer's disease, androgenic alopecia, hypogonadism, hyperpilosity, benign prostate hypertrophy, adenomas or neoplasias of the prostate, treatment of benign or malignant tumor cells containing the androgen receptor, pancreatic cancers, modulation of VEGF expression for use as antiangiogenic agents, osteoporosis, suppressing spermatogenesis, libido, cachexia, endometriosis, polycystic ovary syndrome, anorexia, androgen dependent age-related diseases and conditions, male menopause, male hormone replacement, male and female sexual dysfunction, and inhibition of muscular atrophy in ambulatory patients.
- 10 10. A method for identifying a selective androgen receptor modulator of claim 8, comprising screening a test compound for inhibition of growth of a hormone-dependent tumor cell line and screening said test compound for androgen receptor activity in a nonmalignant cell line containing the androgen receptor, wherein said test compound which inhibits growth of the hormone-dependent tumor cell line while exhibiting no androgen receptor activity or activation of androgen receptor activity in the non-malignant cell line is identified as said selective androgen receptor modulator.
- 20 11. A method for identifying a selective androgen receptor modulator of claim 8, comprising screening a test compound for both inhibition of growth of a hormone-dependent tumor and activation of androgen receptors in other, non-malignant tissues containing the androgen receptor in an animal model bearing said hormone-dependent tumor, wherein a test compound which inhibits growth of the hormone-dependent tumor while exhibiting no androgen receptor activity or activation of androgen receptor activity in the non-malignant tissues of the animal model is identified as said selective androgen receptor modulator.
- 30 12. A molecule or molecular complex of the three-dimensional crystal structure as defined by the structural coordinates of Table A.
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13. A molecule or molecular complex comprising all or any part of the ligand binding site defined by structure coordinates of AR-LBD amino acids V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, 5 R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904, K905, I906 and L907 according to Table A, or a mutant or homologue of said molecule or molecular complex.
- 10 14. The molecule or molecular complex of claim 13 wherein said mutant or homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said AR-LBD amino acids of not more than 1.5 Angstroms or 30% sequence identity with said AR-LBD amino acids.
- 15 15. A molecule or molecular complex comprising all or any part of the ligand binding site defined by structure coordinates of AR-LBD amino acids N705, W741, Q711, R752, F764, T877, M895 and I898 according to Table A, or a mutant or homologue of said molecule or molecular complex.
- 20 16. The molecule or molecular complex of claim 15 wherein said mutant or homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said AR-LBD amino acids of not more than 1.5 Angstroms or 30% sequence identity with said AR-LBD amino acids.
- 25 17. A machine-readable data storage medium comprising a data storage material encoded with machine readable data, wherein the data is defined by the structure coordinates of an AR-LBD/AR-LBD ligand or ligand complex according to Table A or a homologue of said complex, wherein said homologue comprises backbone atoms that have a root mean square deviation from the backbone atoms of the complex of 30 not more than 3.0Å.
18. The machine-readable data storage medium according to claim 17, wherein said AR-LBD/AR-LBD ligand or ligand complex is homologue having a root mean square deviation from the backbone atoms of said amino acids of not more than 2.0 Å.
- 35 19. A machine-readable data storage medium comprising a data storage material encoded with a first set of machine readable data comprising a Fourier

transform of at least a portion of the structural coordinates for an AR-LBD/AR-LBD ligand according to Table A; which, when combined with a second set of machine readable data comprising an X-ray diffraction pattern of a molecule or molecular complex of unknown structure, using a machine programmed with instructions for using said first set of data and said second set of data, can determine at least a portion of the structure coordinates corresponding to the second set of machine readable data, said first set of data and said second set of data.

20. A binding site in AR-LBD for an AR modulator in which a portion of said ligand is in van der Waals contact or hydrogen bonding contact with any portion or all of residues V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, L880, L881, V889, F891, P892, E893, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904, K905, I906 or L907 of AR-LBD according to Table A.

21. The binding site according to claim 20 wherein the AR-LBD is a homologue or mutant with 25%-95% identity to residues V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, L880, L881, V889, F891, P892, E893, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904, K905, I906, or L907 of AR-LBD according to Table A.

22. A computational method of designing an androgen receptor synthetic ligand comprising:
- using a three dimensional model of a crystallized protein comprising an AR-LBD/AR-LBD ligand complex to determine at least one interacting amino acid of the AR-LBD that interacts with at least one first chemical moiety of the AR-LBD ligand; and
 - selecting at least one chemical modification of said first chemical moiety to produce a second chemical moiety with a structure that either decreases or increases an interaction between said interacting amino acid and said second chemical moiety compared to said interaction between said interacting amino acid and said first chemical moiety.

23. A method for identifying a compound that modulates androgen receptor activity, the method comprising any combination of steps of:

- a. modeling test compounds that fit spatially into the AR-LBD as defined by structure coordinates according to Table A, or using a three-dimensional structural model of AR-LBD, mutant AR-LBD or AR-LBD homologue or portion thereof;
- b. using said structure coordinates or ligand binding site as set forth in claim 20 to identify structural and chemical features;
- c. employing identified structural or chemical features to design or select compounds as potential SARMs;
- d. employing the three-dimensional structural model or the ligand binding site to design or select compounds as potential SARMs;
- e. synthesizing the potential SARMs;
- f. screening the potential SARMs in an assay characterized by binding of a test compound to the AR-LBD; and
- g. modifying or replacing one or more amino acids from AR-LBD selected from the group consisting of V685, L700, L701, S702, S703, L704, N705, E706, L707, G708, E709, Q711, A735, I737, Q738, Y739, S740, W741, M742, G743, L744, M745, V746, F747, A748, M749, G750, R752, Y763, F764, A765, L768, F770, M780, M787, I869, L873, H874, F876, T877, F878, L880, L881, V889, F891, P892, E893, M894, M895, A896, E897, I898, I899, S900, V901, Q902, V903, P904, K905, I906 or L907 of AR-LBD according to Table A.

24. A pharmaceutical composition comprising a selective androgen receptor modulator and a pharmaceutically acceptable carrier, wherein said selective androgen receptor modulator is selected or designed in accordance with the method of claims 10, 11, 22 or 23.